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10/583,464	01/16/2007	Rasappa G. Arumugham	025721-000110US	4012

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EXAMINER
LE, EMILY M

ART UNIT	PAPER NUMBER
1648	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/583,464	ARUMUGHAM ET AL.	
	Examiner	Art Unit	
	EMILY M. LE	1648	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *06/16/2006, 01/16/2007 + 04/29/2009*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *370-401* is/are pending in the application.

4a) Of the above claim(s) *370-383 and 397-401* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *384-396* is/are rejected.

7)☒ Claim(s) *384-391* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *08/20/08, 02/17/09, 04/13/09 and 10/30/2009*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Election/Restrictions

1. Applicant's election without traverse of Group II in the reply filed on 03/05/2009 is acknowledged.

Status of Claims

2. Claims 1-369 are cancelled. Claims 370-401 are pending. Claims 370-383 and 397-401 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected invention, there being no allowable generic or linking claim. Election was made **without** traverse in the reply filed on 03/05/2009. Claims 384-396 are under examination.

Claim Objections

3. Claims 384-391 are objected to because of the following informalities: the subscripted "P" in the recited formula should be in lower case, "p". Appropriate correction is required.

Claim Rejections - 35 USC § 112

4. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

5. Claims 388-396 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

It is unclear what the metes and bounds of the cited claims are as the claims recite dependency to withdrawn claim, claim 377.

Claim Rejections - 35 USC § 102

6. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

7. Claims 384-385, 387-389, 391-393 and 395 are rejected under 35 U.S.C. 102(b) as being anticipated by Conley et al.[1]

The claims are directed to a peptide immunogen-protein/peptide carrier conjugate wherein the protein carrier has a capping molecule. Claim 385, which depends on claim 384 requires the protein/polypeptide carrier to be selected from the group consisting of serum albumin, keyhole limpet hemocyanin (KLH), immunoglobulin molecules, thyroglobulin, ovalbumin, influenza hemagglutinin, PADRE polypeptide, malaria circumsporozite (CS) protein, hepatitis B surface antigen, Heat Shock Protein 65, Mycobacterium tuberculosis, cholera toxin, cholera toxin mutants with reduced toxicity, diphtheria toxin, CRM_{197} protein that is cross reactive with diphtheria toxin, recombinant Streptococcal C5a peptidase, Streptococcus pyogenes ORF1224, Streptococcus pyogenes ORF1664, Streptococcus pyogenes ORF2452, Chlamydia pneumoniae ORF T367, Chlamydia pneumoniae ORF T858, Tetanus toxoid, HIV gp120 T1, components recognizing microbial surface adhesive matrix molecules, growth factors, hormones, cytokines and chemokines. Claim 387, which depends on claim 384, requires the peptide immunogen be selected from the group consisting of bacterial

[1] Conley et al. WO 02/93804, published December 13, 2001.

protein, a viral protein and a eukaryotic protein. Claim 388 is directed to the invention encompassed by claim 384. Claim 392 is directed to the invention encompassed by claim 384, with the exception that the claim does not require capping and does require that the conjugate comprises one or more pharmaceutically acceptable excipients, diluents and/or adjuvants. Claims 389 and 391, and 393 and 395, which depend on claims 388 and 392, respectively, recite the limitations of claims 385 and 387, respectively.

Conley et al. teaches a composition comprising peptide immunogen-protein/peptide carrier conjugate, wherein the protein carrier has a capping molecule. [Example 2, page 22, in particular.] The protein/polypeptide carriers that Conley et al. teaches include serum albumin, hepatitis B surface antigen, diphtheria toxin, Tetanus toxoid. [Lines 14-20, page 8, in particular.] The peptide immunogen of Conley et al. is a viral protein. The composition of Conley et al. also comprises one or more pharmaceutically acceptable excipients, diluents and/or adjuvants. [Examples 2 and 5, pages 22 and 25, in particular.] In the instant case, Conley et al. teaches the claimed invention. Therefore, the claimed invention is anticipated by Conley et al.

8. Claims 392-395 are rejected under 35 U.S.C. 102(b) as being anticipated by Mariotti et al.[2]

The claims are directed to composition comprising a peptide immunogen-protein/peptide carrier conjugate, wherein the conjugate comprises one or more pharmaceutically acceptable excipients, diluents and/or adjuvants. Claim 393, which

depends on claim 384 requires the protein/polypeptide carrier to be selected from the group consisting of serum albumin, keyhole limpet hemocyanin (KLH), immunoglobulin molecules, thyroglobulin, ovalbumin, influenza hemagglutinin, PADRE polypeptide, malaria circumsporozite (CS) protein, hepatitis B surface antigen, Heat Shock Protein 65, Mycobacterium tuberculosis, cholera toxin, cholera toxin mutants with reduced toxicity, diphtheria toxin, CRM_{197} protein that is cross reactive with diphtheria toxin, recombinant Streptococcal C5a peptidase, Streptococcus pyogenes ORF1224, Streptococcus pyogenes ORF1664, Streptococcus pyogenes ORF2452, Chlamydia pneumoniae ORF T367, Chlamydia pneumoniae ORF T858, Tetanus toxoid, HIV gp120 T1, components recognizing microbial surface adhesive matrix molecules, growth factors, hormones, cytokines and chemokines. Claim 394, which deepens on claim 393, requires the protein/polypeptide carrier be CRM_{197}. Claim 395, which depends on claim 392, requires the peptide immunogen be selected from the group consisting of bacterial protein, a viral protein and a eukaryotic protein.

Mariotti et al. teaches a composition comprising peptide immunogen-protein/peptide carrier conjugate, wherein the composition comprises one or more pharmaceutically acceptable excipients, diluents and/or adjuvants. The protein/polypeptide carrier that Mariotti et al. teaches is CRM_{197}. The peptide immunogen of Mariotti et al. is a viral protein. The composition of Mariotti et al. also comprises one or more pharmaceutically acceptable excipients, diluents and/or

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[2] Mariotti et al. Immunogenicity of anti-Haemophilus influenzae type b CRM_{197} conjugate following mucosal vaccination with oligodeoxynucleotide containing immunostimulatory sequences as adjuvants. Vaccine, May 2002, Vol. 20, 2229-2239.

adjuvants. In the instant case, Mariotti et al. teaches the claimed invention. Therefore, the claimed invention is anticipated by Mariotti et al.

Claim Rejections - 35 USC § 103

9. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

10. Claims 392 and 396 are rejected under 35 U.S.C. 103(a) as being unpatentable over Conley et al., as applied to claim 392.

Claim 396, which depend on claim 392, requires that the one or more adjuvants be selected from the group consisting of GM-CSF, 529 SE, IL-12, aluminum phosphate, aluminum hydroxide, Mycobacterium tuberculosis, Bordetella pertussis, bacterial lipopolysaccharides, aminoalkyl glucosamine phosphate compounds, MPL™, a polypeptide, Quil A, STIMULON™ QS-21, a pertussis toxin, an E. coli heat-labile toxin, IL-1 alpha, IL-1 beta, IL-2, IL-4, IL-5, IL-6, IL-7, IL-8, IL-10, IL-13, IL-14, IL-15, IL-16, IL-17, IL-18, interferon-alpha, interferon-beta, interferon-gamma, G-CSF, TNF-alpha and TNF-beta.

The significance of Conley et al., as applied to claim 392 is provided above. As noted above, Conley et al. does teach the inclusion of an adjuvant with a composition comprising peptide immunogen-protein/peptide carrier conjugate, wherein the protein carrier has a capping molecule. The adjuvant used by Conley et al. in said composition is not any of those recited in the claims. However, Conley et al. does teach the use of

adjuvants with the composition. Conley et al. also teaches the following adjuvants: alum, AlPO.sub.4, alhydrogel, Lipid-A and derivatives or variants thereof, Freund's complete or incomplete adjuvant, neutral liposomes, liposomes containing vaccine and cytokines or chemokines. Thus, at the time the invention was made, it would have been prima facie obvious for one of ordinary skill in the art, at the time the invention was made, to include any of the listed adjuvants with the composition of Conley et al. One of ordinary skill in the art, at the time the invention was made, would have been motivated to do so to enhance the immune response induced by the composition of Conley et al. One of ordinary skill in the art, at the time the invention was made would have had a reasonable expectation of success for doing so because the use of adjuvants in pharmaceuticals is routinely practiced.

11. Claims 384-386, 388-390 and 392-394 are rejected under 35 U.S.C. 103(a) as being unpatentable over Conley et al., as applied to claims 384-385, 388-389 and 392-393, in view of Mariotti et al.

Claims 386, which depends on claim 385, requires the protein/polypeptide carrier be CRM_{197}. Claims 390 and 390, which depend on claims 389 and 393, respectively, recites the limitation of claim 386.

The significance of Conley et al., as applied to claims 384-385, 388-389 and 392-393 is provided above. While Conley et al. does teach the use of protein/polypeptide carrier, Conley et al. does not teach the use of CRM_{197} as a protein/polypeptide carrier. However, it is noted that Conley et al. does set forth the use of protein/polypeptide carrier to enhance the immune response induced against a peptide antigen. At the time

the invention was made, Mariotti et al. teaches the use of CRM_{197} as a protein/polypeptide carrier to enhance the immune response of a peptide antigen. Thus, at the time the invention was made, it would have been prima facie obvious for one of ordinary skill in the art to use CRM_{197} as the protein/polypeptide carrier in the composition of Conley et al. One of ordinary skill in the art, at the time the invention was made would have been motivated to do so to enhance the immune response induced by the peptide antigen. One of ordinary skill in the art, at the time the invention was made would have had a reasonable expectation of success for doing so because the use of CRM_{197} as a carrier is well established in the art by Mariotti et al.

12. Claims 384-391 are rejected under 35 U.S.C. 103(a) as being unpatentable over Mariotti et al., in view of Conley et al.

The claims are directed to a peptide immunogen-protein/peptide carrier conjugate wherein the protein carrier has a capping molecule. Claim 385, which depends on claim 384 requires the protein/polypeptide carrier to be selected from the group consisting of serum albumin, keyhole limpet hemocyanin (KLH), immunoglobulin molecules, thyroglobulin, ovalbumin, influenza hemagglutinin, PADRE polypeptide, malaria circumsporozite (CS) protein, hepatitis B surface antigen, Heat Shock Protein 65, Mycobacterium tuberculosis, cholera toxin, cholera toxin mutants with reduced toxicity, diphtheria toxin, CRM_{197} protein that is cross reactive with diphtheria toxin, recombinant Streptococcal C5a peptidase, Streptococcus pyogenes ORF1224, Streptococcus pyogenes ORF1664, Streptococcus pyogenes ORF2452, Chlamydia pneumoniae ORF T367, Chlamydia pneumoniae ORF T858, Tetanus toxoid, HIV gp120

T1, components recognizing microbial surface adhesive matrix molecules, growth factors, hormones, cytokines and chemokines. Claim 387, which depends on claim 384, requires the peptide immunogen be selected from the group consisting of bacterial protein, a viral protein and a eukaryotic protein. Claim 388 is directed to the invention encompassed by claim 384.

Mariotti et al. teaches a composition comprising peptide immunogen-protein/peptide carrier conjugate. The protein/polypeptide carrier that Mariotti et al. teaches is CRM_{197}. The peptide immunogen of Mariotti et al. is a viral protein.

It is not readily apparent if the protein carrier of Mariotti et al. has a capping molecule. However, at the time the invention was made, Conley et al. teaches the use of capping molecules to inhibit the ability of the linker reactive group to which it is attached to undergo further reaction.[Lines 4-11, page 11, in particular.] Thus, at the time the invention was made, it would have been prima facie obvious for one of ordinary skill in the art to include a capping molecule. One of ordinary skill in the art, at the time the invention was made would have been motivated to do so to inhibit the ability of the linker reactive group to which it is attached to undergo further reaction. One of ordinary skill in the art, at the time the invention was made, would have had a reasonable expectation of success for doing so because Conley et al. demonstrates that capping molecules is routinely practiced.

Double Patenting

13. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the

unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA $_{197}$0); and In *re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

14. Claims 384-396 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claim 398 of copending Application No. 10/583503. Although the conflicting claims are not identical, they are

not patentably distinct from each other because both sets of claims are directed to a peptide immunogen conjugated to a protein carrier.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Conclusion

15. No claim is allowed.

16. Any inquiry concerning this communication or earlier communications from the examiner should be directed to EMILY M. LE whose telephone number is (571)272-0903. The examiner can normally be reached on Monday - Friday, 8 am - 5:30 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Larry R. Helms can be reached on (571) 272-0832. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9_{197} (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/EMILY M LE/

Primary Examiner, Art Unit 1648

/E. M. L./
Primary Examiner, Art Unit 1648